REMARKS

In the Office Action dated July 16, 2007 the Examiner has objected to the specification with reference to the sequence listing, and also to the abstract of the above referenced application. The Examiner has also rejected Applicants' claims as lacking novelty and being obvious. Applicants traverse each of the Examiner's rejections, as detailed below.

Applicants have cancelled claims 1 and 3. Claim 2 has been amended to include additional limitations that find support in claim 3 canceled herein and in the application as filed. In particular, the amended definitions of the groups X, m, n, and Y are supported by original claims 3 and 10 and the Examples. Claim 12 has been amended to correct a spelling error. No new matter has been introduced by way of these amendments.

Objection To The Abstract Under 37 C.F.R. § 1.72

Applicants have amended the abstract to incorporate the Examiner's suggestions and accordingly request that the objection to the Abstract is withdrawn.

Objection To The Specification Under 37 C.F.R. § 1.821-825

Applicants point out to the Examiner that the sequence disclosure requirements under 37 C.F.R. § 1.821-825 have been complied with and draw Examiner's attention to the Sequence Listing filed on September 22, 2004, and the Preliminary Amendment filed on the same date adding the required sequence identification information to the specification. Accordingly, Applicants respectfully request that the objection to the specification is withdrawn.

Claim Rejections – 35 U.S.C § 102

The Examiner has rejected Claims 1-6 under 35 USC § 102(b) as being anticipated by Vu, et al., Bioconjugate Chem. *6*:599-607 (1995) ("Vu"). In particular, the Examiner refers to compound 32 disclosed in Vu. It is well-settled law that in order for a reference to anticipate a claim under Section 102 of the Patent Law, that "A claim is anticipated only if each and every element as set forth in the claim is found, either expressly or inherently described, in a single prior art reference." *Verdegaal Bros. v. Union Oil Co. of California*, 814 F.2d 628, 631, 2 USPQ2d 1051, 1053 (Fed. Cir. 1987), MPEP 2131.

Applicants have canceled claim 1. In addition, Applicants have amended claims 2 and 4-6 to require that "m is 5" and that "Y is-NHC(O)CF_3." In the cited compound 32 of Vu relied upon by the Examiner, the group attached to the corresponding nitrogen is the tripeptide –Gly-Gly-Gly-, which is in turn protected as a phthalimide. That tripeptide group is not included in the compounds recited in Applicants' claims. Therefore, Applicants' invention requiring the corresponding aminocaproic acid fragment protected with trifluoroacetyl cannot be anticipated by Vu and Applicants request that Examiner reconsider the rejection of Applicants' claims 1-6 under 35 USC § 102(b) leading to its withdrawal.

The Examiner has also rejected Claims 1-6 under 35 USC § 102(b) as being anticipated by Mullah, et al., U.S. Patent No. 5,736,626, , ("Mullah"). In the cited compounds 11 and 12 of Mullah, relied upon by the Examiner, the group attached to the corresponding nitrogen is an aminocaproic acid residue protected by a fluorenyloxycarbonyl fragment. The fluorenyloxycarbonyl fragment is not included in the compounds recited in Applicants' claims. Further, in the cited compound 13, relied upon by the Examiner, the nitrogen of the aminocaproic acid fragment has no attached protecting group. The unprotected amino group of the aminocaproic acid fragment is not included in the Applicants' claims. Therefore, Applicants' invention requiring the corresponding aminocaproic acid fragment protected with trifluoroacetyl cannot be anticipated by Mullah and Applicants request that Examiner reconsider the rejection of Applicants' claims 1-6 under 35 USC § 102(b) leading to its withdrawal.

Claim Rejections – 35 U.S.C § 103(a)

The Examiner has rejected Claims 1- 6 and 10-12 under 35 USC § 103(a) as being unpatentable over Mullah in view of Vu. Applicants suggest that the Examiner has misread the disclosures of both Mullah and Vu and improperly considered those disclosures in a piece-meal fashion. The Examiner has failed to consider the disclosure of Vu in its entirety contrary to MPEP 2141.03 (VI.)

> A prior art reference must be considered in its entirety, i.e., as a whole, including portions that would lead away from the claimed invention. *W.L. Gore & Associates, Inc. v. Garlock, Inc.*, 721 F.2d 1540, 220 USPQ 303 (Fed. Cir. 1983), *cert. denied*, 469 U.S. 851 (1984)

Examiner correctly points out that Mullah does not teach the use of the chemical group TFA for modification of the 5-aminopentyl chemical group [$(CH_2)_5NH_2$]. The compounds of Mullah are directed to methods in which modification of a linker with a chemical group that allows easy detection, for example, a fluorescent tag, prior to oligonucleotide elaboration. Moreover, Mullah teaches away from post-oligonucleotide-elongation modification and describes, in detail, a rationale for avoiding such modifications in column 1, line 30 to line 45, stating

> "The most effective and convenient method for introducing a label at the 3'-end of a synthetic polynucleotide is to use a direct labeling method utilizing an appropriately functionalized synthesis support because, (i) direct methods do not require a post-synthesis reaction step, thereby simplifying the synthesis of 3'-labeled polynucleotides; and (ii) direct methods avoid the problems associated with the low reaction yield (<60%) typically encountered when an amino-labeled oligonucleotide is reacted with a label, e.g., a dye-NHS-ester label, namely: (a) purification of the labeled oligonucleotide away from excess label; (b) purification of the labeled oligonucleotide away from unlabeled oligonucleotide; (c) increased costs associated with the low product yield caused by throwing away the large fraction of unlabeled oligonucleotides; and (d) irreversible capping of the 3'-amine functionality during synthesis."

Consequently, they describe the use of chemical groups that can be easily removed, "FMOC, tBOC or other like nitrogen protecting groups" in the presence of the DMT protected terminal alcohol. Notably, they list only carbamate-type protecting groups which are substantially unlike the TFA protecting group in the chemistry of their removal and the mildness of the conditions required to remove them, as is well known in the art of organic synthesis, see for example Greene, T. W., Wuts, P. G. M. (1999) Protective Groups in Organic Chemistry, Third Edition, Wiley-Interscience, New York, NY. Thus, in order to use the teachings of Mullah, it is inapposite to use a protecting group on the nitrogen that cannot be removed in the present of the DMT group. Such a modification of Mullah prevents the very synthetic process taught, namely the elaboration of the nucleotide prior to the incorporation of the label on the terminal hydroxyl group.

Even so, the Examiner turns to Vu for its teachings of the TFA protection group. However, Applicants believe that the Examiner has improperly relied upon Vu because Vu also dissuades the skilled artisan from using the TFA group, but for a different reason. In particular, the Examiner cites the use of the TFA group in Vu in compound 19 in Figure 1, page 604 as

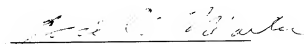
providing motivation to use the TFA group with the disclosure of Mullah to provide Applicants' invention.

However, Vu teaches that for the purposes of delivering linkers capable of so-called 3'-amino modification after oligonucleotide elongation, the TFA group is unsuitable. They disclose that use of the TFA group in their synthetic sequence leads to the crude oligonucleotide mixture containing over 25% of materials derived from premature loss of the TFA group compared to no detectable levels of such products when one uses the phthaloyl protecting group that is the focus of their disclosure. A careful reading of the disclosure of Vu reveals that Vu, et al., teach away from the use of the TFA group for the purpose that Applicants have disclosed. Therefore, like Mullah above, Vu does not motivate the person of ordinary skill in the art to use the TFA protecting group in any context.

The Examiner has attempted to render obvious Applicants' claims asserting that the skilled artisan would modify the teachings of Mullah with those of Vu, notwithstanding, the teaching away by both references of the TFA protecting group. Applicants believe that the combination of Mullah and Vu is improper. Mullah is directed to appending an oligonucleotide modifying group during the beginning stages of synthesis, the direct method, and requires the use of protecting groups that can be removed at that early stage of synthesis under mild conditions in the presence of DMT alcohol protecting group. Vu, on the contrary, is directed to synthesizing the oligonucleotide first and subsequently attaching the modifying group, the indirect method, and requires a protecting group that is stable to the conditions associated with multiple chain-extension chemistry cycles. Consequently, the teachings of Vu and Mullah require amino protecting groups with contradictory and incompatible requirements. Therefore, there cannot be any motivation provided by either reference to modify the teachings of Mullah with those of Vu to include the TFA protecting group required in Applicants' invention. Applicants' request that the Examiner withdraw the rejection of the claims under 35 USC § 103(a).

Based upon the foregoing amendments and remarks, Applicants believe the claims are in now in condition for allowance. Applicants respectfully request that all outstanding objections and rejections be withdrawn, and that the application is passed to issue.

Respectfully submitted,
BARNES & THORNBURG LLP



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Date: December 17, 2007